IUCLID

Data Set

Existing Chemical	:	ID: 108-20-3
CAS No.	:	108-20-3
EINECS Name	:	diisopropyl ether
EC No.	:	203-560-6
TSCA Name	:	Propane, 2,2'-oxybis-
Molecular Formula	:	C6H14O

Producer related part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	18.05.2005

Substance related part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	18.05.2005
Status	:	
Memo	:	HPV
Printing date	:	02.02.2008
Revision date	:	
Date of last update	:	02.02.2008
Number of pages	:	61
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	**:**	
Substance type	**:**	organic
Physical status	**:**	liquid
Purity	**:**	
Colour	**:**	
Odour	**:**	

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1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

2,2'-oxybis-propane

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2,2'-oxybispropane

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2-Isopropoxy Propane

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2-Isopropoxypropan

27.10.2005

2-isopropoxypropane

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Diisopropyl Ether

27.10.2005

Dipropyloxid

27.10.2005

IPE

27.10.2005

IPE; Diisopropylether; DIPE; 2-Isopropoxy propane

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Isopropyl Ether

27.10.2005

Isopropylether

27.10.2005

propane, 2,2'-oxybis-

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1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= -86.8 °C
Sublimation	:	
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Test substance	:	CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability	:	(2) valid with restrictions The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag	:	Critical study for SIDS endpoint

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2.2 BOILING POINT

Value	:	= 68.5 °C at 1013 hPa
Decomposition	:	
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropylether
Test substance	:	CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability	:	(2) valid with restrictions The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag	:	Critical study for SIDS endpoint

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2.3 DENSITY

Type	:	density
Value	:	= .7241 g/cm³ at 20 °C
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Test substance	:	CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability	:	(2) valid with restrictions The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag	:	Critical study for SIDS endpoint

07.12.2005 (25)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= 198.65 hPa at 25 °C
Decomposition	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Method	:	Method not specified.
Test substance	:	CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data were not reviewed for quality, however, the reference is from a peer-reviewed handbook.
Flag	:	Critical study for SIDS endpoint

07.12.2005 (9)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 1.52 at 25 °C
pH value	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropylether
Method	:	Method not specified.
Test substance	:	CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability	:	(2) valid with restrictions The value cited by the authors is a measured and preferred value. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag	:	Critical study for SIDS endpoint

27.10.2005 (19)

Partition coefficient	:	octanol-water
Log pow	:	= 2.4 at °C
pH value	:	6.7
Method	:	other (calculated): Indirect method by reverse-phase HPLC
Year	:	
GLP	:	no
Test substance	:	other TS: diisopropyl ether (CAS No. 108-20-3)
Result	:	Log Pow = 2.4 (Pow = 250) at pH 6.7
Test condition	:	The HPLC system was a reverse-phase C18-coated silica gel column, 250 mm x 5 mm id, with a mobile phase of 3 volumes methanol and 1 volume water (final pH 6.7) at a flow rate of 1 mL/min. 100 mL samples of an approximate 1 mg/mL solution in the mobile phase were injected, and the emergence of the material was observed using refraction index detection. Thirty-one reference compounds were used to generate the linear relationship between log k (k = capacity factor) and log Pow. Using the HPLC retention time for the peak of the test substance, the log k was determined, and the log Pow value was calculated using the linear equation developed from the reference compounds. Log Pow was determined according to the following calculations: Retention time (RT), min = 5.7

Capacity factor, k = 0.87, k = (RTcmpd - RTunretained std)/RTunretained std
log k = -0.06
linear equation: log k = -0.930 + 0.357 log Pow

Reliability : (1) valid without restriction
12.12.2005 (11)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 8800 mg/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)

Test substance : CAS No. 108-20-3; diisopropyl ether; purity is unknown.
Reliability : (2) valid with restrictions
The Ullmann's Encyclopedia of Industrial Chemistry is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag : Critical study for SIDS endpoint
07.12.2005 (17)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Conc. of substance	:	at 25 °C
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .00000000002434 cm³/(molecule*sec)
Degradation	:	= 50 % after 5.3 hour(s)
Deg. product	:	
Method	:	other (calculated): Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.12
Year	:	
GLP	:	
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Method	:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.12 Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson under the following conditions: Temperature: 25°C Sensitizer: OH- radical Concentration of Sensitizer: 1.5E6 OH- radicals/cm3
Remark	:	DIPE has the potential to volatilize to air, based on a vapor pressure of 19,865 Pa at 25°C (Daubert and Danner, 1989), where it is subject to atmospheric oxidation. In air, DIPE can react with photosensitized oxygen in the form of hydroxyl radicals (OH-). The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 2000) calculates a chemical half-life for a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated), based on an OH-reaction rate constant and a defined OH- concentration. DIPE has a calculated half-life in air of 5.3 hours or 0.4 days (12-hour day), based on a rate constant of 24.34 E-12 cm3/molecule*sec and an OH-concentration of 1.5 E5 OH-/cm3.
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag	:	Critical study for SIDS endpoint
07.12.2005		(15)
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Method	:	Technical discussion
Remark	:	Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance in aqueous solution. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet

(UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer (Harris, 1982a).
An approach to assessing the potential for a substance to undergo photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by constituent molecules (Zepp and Cline, 1977). The oxygen non-bonding electrons in ethers do not give rise to absorption above 160 nm, which is why pure ether solvents can be used in spectroscopic studies.
Consequently, DIPE is not subject to photolytic processes in the aqueous environment.

Reliability : (2) valid with restrictions
This robust summary has a reliability of 2 because it is a technical discussion and not a study.

Flag : Critical study for SIDS endpoint
07.12.2005 (48)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method : other: Technical discussion
Year :
GLP : no data
Test substance : other TS: Diisopropyl Ether (CAS # 108-20-3)

Result : Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals with leaving groups that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Gould, 1959). The lack of a suitable leaving group renders a compound resistant to hydrolysis. DIPE is resistant to hydrolysis because it lacks a functional group that is hydrolytically reactive and Harris (1982b) identifies ether groups as generally resistant to hydrolysis. Therefore, hydrolysis will not contribute to the removal of diisopropyl ether from the environment.

Reliability : (2) valid with restrictions
This robust summary has a reliability of 2 because it is a technical discussion and not a study.

Flag : Critical study for SIDS endpoint
07.12.2005 (18) (20)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type :
Media : other: air - biota - sediment(s) - soil - water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation according Mackay, Level I
Year :

Remark : Physicochemical data used in the calculation:

Parameter Value w/ Units

Molecular Weight = 102.18
Temperature = 25° C
Log Kow = 1.52
Water Solubility = 8,800 g/m3
Vapor Pressure = 19,865 Pa
Melting Point = -86.8° C

Result : Using the Mackay Level I calculation, the following distribution is predicted for diisopropyl ether:

%Distribution	Compartment
97.83	Air
2.10	Water
0.06	Soil
<0.01	Sediment
<0.01	Suspended Sediment
<0.01	Biota

Test substance : Diisopropyl Ether (CAS # 108-20-3)
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint
07.12.2005 (28)

Type : fugacity model level III
Media : other
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Level III simulation using the Mackay Multimedia Environmental Model (Mackay, 2001)
Year :

Method : Level III simulation using the Mackay Multimedia Environmental Model (Mackay, 2001). Mass balances are calculated for the four bulk media of air (gas + aerosol), water (solution + suspended sediment + biota), soil, (solids + air + water), and sediment (solids + pore water). Equilibrium exists within, but not between media. Physical-chemical properties are used to quantify a chemical's behavior in an evaluative environment. Three types of chemicals are treated in this model: chemicals that partition into all media (Type 1), non volatile chemicals (Type 2), and chemicals with zero, or near-zero, solubility (Type 3). The model can not treat ionizing or speciating substances. The Level III model assumes a simple, evaluative environment with user-defined volumes and densities for the following homogeneous environmental media (or compartments): air, water, soil, sediment, suspended sediment, fish and aerosols.

This model provides a description of a chemical's fate including the important degradation and advection losses and the intermedia transport processes. The distribution of the chemical between media depends on how the chemical enters the system, e.g. to air, to water, or to both. This mode of entry also affects persistence or residence time.

The rates of intermedia transport are controlled by a series of 12 transport velocities. Reaction half-lives are requested for all 7 media. The advective residence time selected for air also applies to aerosols and the residence time for water applies to suspended sediment and fish. The advective residence time of aerosols, suspended sediment and fish cannot be specified independently of the air and water residence times.

Result : Output

	Mass%	Half life(hr)	Emissions(kg/hr)
Air	19.4	25.2	1000
Water	61.0	360	1000
Soil	19.5	720	1000
Sediment	0.1	3240	0

Test condition : Physchem Inputs
Molar Mass = 102.18
Data Temperature = 25 ºC
Water Solubility = 8800 mg/l exp.
Vapour Pressure = 19865 Pa exp.
Log Kow = 1.52 exp.
Melting Point = -86.8 ºC exp.

Reaction Half Lives in hours (if not available they can be predicted using EPIWIN)

Air (gaseous)	25.2
Water (no susp. part.)	360
Bulk Soil	720
Bulk Sediment	3240
Suspended Particles	360
Fish	360
Aerosol	25.2

Environmental Properties (EQC standard environment)
Dimensions (all defaults)
Densities (all defaults)
Organic carbon & Advection (all defaults)
Transport Velocities (all defaults)

Emission and Inflows (defaults used)
Air 1000 kg/hr
Water 1000 kg/hr
Soil 1000 kg/hr
Sediment 0 kg/hr

Test substance : Diisopropyl Ether, CAS No. 108-20-3

Conclusion : The majority of DIPE is calculated to partition into the water phase, with smaller but significant amounts into air and soil, based on the modeling parameters used in this calculation. DIPE is considered to be a Type 1 chemical with potential to partition into all environmental compartments.

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

Flag : Critical study for SIDS endpoint
01.11.2005 (27) (29) (30) (31)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Contact time	:	28 day(s)
Degradation	:	(±) % after
Result	:	other: not readily biodegradable
Deg. product	:	
Method	:	OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year	:	1982
GLP	:	no
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Result :

Test substance was not readily biodegradable. After 28 days, the test substance exhibited no measurable biodegradation. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the testing guideline were noted. The inhibition study showed that the test substance did not inhibit the biodegradability of the positive control substance, sodium benzoate.

Sample	% Degradation* Mean (day 28)	% Degradation (day 28)
Test Substance	0.0, 0.0	0.0
Na Benzoate	65.0, 73.0	69.0

* duplicate data

Mean oxygen concentrations (mg/L) of duplicate test systems:

Day 0
Mineral Salts Control = 8.85
Blank = 8.8
Na Benzoate = 8.95
Test Substance = 8.9 (single test system)
Test Substance + Na Benzoate = 8.9* (single test system)

Day 5
Mineral Salts Control = 9.0
Blank = 8.8
Na Benzoate = 5.7
Test Substance = 8..85
Test Substance + Na Benzoate = 5.8

Day 15
Mineral Salts Control = 8.75
Blank = 8.65
Na Benzoate = 4.9
Test Substance = 8.55
Test Substance + Na Benzoate = 4.9

Day 28
Mineral Salts Control = 8.65
Blank = 7.05
Na Benzoate = 3.6
Test Substance = 8.3
Test Substance + Na Benzoate = 4.15

Test condition : The inoculum source was the Sittingbourne Sewage works in Kent,

England, and was prepared according to methods described in the OECD 301D guideline. The test substance was added to the test medium by direct addition at a concentration of 3.0 mg/L. Test systems were incubated at 20 ± 1 °C and biodegradation was determined by measuring the oxygen concentration on days 5, 15, and 28. Each sampling of the test substance and control was conducted in duplicate. The theoretical oxygen demand was 2.82 mg O2 per mg test substance and a theoretical carbon dioxide (CO2) evolution of 2.59 mg CO2 per mg test substance. Sodium benzoate was used as the positive control.

The purity of the test substance was not supplied, but the infra-red spectrum of the test substance matched a published standard (density = 0.723 to 0.726 kg/L). The test substance was stored in the dark at ambient temperature. Nitrogen was blown over the surface of the material when the container was opened and exposed to air in order to minimize peroxide formation.

Conclusion : Diisopropyl ether is not readily biodegradable and it did not significantly inhibit the biodegradability of the test substance in an inhibition test.

Reliability : (1) valid without restriction

07.12.2005 (42)

Type :
Inoculum : other: sanitary waste treatment plant effluent
Contact time : 5 day(s)
Degradation : (±) % after
Result :
Deg. product :
Method : other: American Public Health Association; No. 219 5-Day BOD; Standard Dilution Method
Year : 1971
GLP : no
Test substance : other TS: diisopropyl ether (CAS No. 108-20-3)

Remark : Test type: Biological Oxygen Demand (BOD)
Result : 0.19 g O2/g test material at 20 ± 1°C
The theoretical oxygen demand (ThOD) of the test substance was 2.82. The percent ThOD in 5 days was 7%.

The article stated that the only deviation from the standard method was the addition of 0.5 mg/L allylthiourea to prevent nitrification.

Test condition : The article stated that the test method followed APHA Standard Method No. 219 (1971). The test was run at a temperature of 20 ± 1°C. 500-mL test solutions were seeded with a filtered 10-mL volume of the effluent from a biological sanitary waste treatment plant. The activity of the inoculum was check by including a treatment containing a mixture of glucose and glutamic acid. Test mixtures were stirred using a magnetic stirrer.

Conclusion : 5-day BOD = 0.19 g/g, representing 7% biodegradation of the test substance.

Reliability : (2) valid with restrictions
The article presented a brief description of the testing methods, but cited a reliable guideline method in use at the time of the study.

07.02.2006 (2)

Type : aerobic
Inoculum : activated sludge
Deg. product :
Method : other: (comparison study of three aerobic biodegradation methods)
Year : 1997
GLP : no
Test substance : other TS: diisopropyl ether (CAS No. 108-20-3)

Method : Comparison study of three aerobic biodegradation methods)

Continuous Biological Treatment:
(1) EPA Method 304B (EPA, 1994)
Batch Methods:
(2) Batch Oxygen addition (BOX) (Rajagopalan et al., 1998), and
(3) Serum Bottle Test (SBT) (Rajagopalan et al., 1998)

Remark : Exposure Period:
Method 304: 30 days
BOX: 0.5 to 2 hours
SBT: 0.5 to 2 hours

Result : The average percent removal of the test substance in the continuous activated sludge unit (EPA Method 304B) was 99.4%.

Three experimental trial runs with each of the three biodegradation methods yielded the following average first-order biodegradation rate constants (K1 = L/g Volatile Suspended Solids-h) for the test substance:

	K1 (L/g VSS-h)
304B	98
BOX	17.4
SBT	19.2

Test condition : A pilot-scale continuous activated sludge unit served as the source of biomass for kinetic rate constant comparisons of the three methods. The activated sludge was acclimated in the pilot unit by feeding a synthetic cocktail of eight volatile organic compounds during a 2-month equilibration period. Equilibration and testing was done at ambient temperature (22 to 24°C). The hydraulic retention time (HRT) was 7.7 hours and the solids retention time (SRT) was 33 days. Average organic removal efficiencies based on COD and TOC were 92 and 88%, respectively.

During the biodegradation testing using Method 304B, feed and effluent samples were collected in headspace-free VOA vials and stored at 4°C until analyzed. Samples were analyzed by purge-and-trap gas chromatography using a flame ionization detector. Triplicate biodegradation runs on the test compound were conducted with at least six influent and effluent samples taken at 1 HRT (approx. 8 hours) intervals.

The two batch biodegradation testing methods (BOX and SBT) used activated sludge biomass from the pilot-scale reactor. Biomass was diluted using effluent from the system to achieve range of 200 to 600 mg/L. The test compound was injected into the batch reactors and the concentration was monitored over time by collecting gas samples directly from the headspace using an automatic sampling pump and analyzing immediately using gas chromatography.

Conclusion : The authors indicated that K1 values >10 L/g VSS-h represent readily biodegradable organic compounds. Based on the results of this study, all three test methodologies showed the test substance to be effectively utilized by activated sludge microorganisms under aerobic conditions.

Reliability : (2) valid with restrictions
The publication presented a well-documented study based on ound scientific principles.

07.02.2006 (6) (34) (44)

Type : aerobic
Inoculum : other: Mixture (see remarks)
Contact time : 600 day(s)
Degradation : (±) % after
Result :
Deg. product :
Method : other: (continuous-flow bioreactors)
Year : 2001
GLP : no
Test substance : other TS: diisopropyl ether (CAS No. 108-20-3)

Remark	:	Inoculum consisted of a mixture of the following: 1) mixed liquor from the Metropolitan Sewer District (MSD), Cincinnati, OH, 2) mixed liquor from Shell Development Co., Houston, TX, and 3) aquifer material wash water from a MTBE-contaminated site in Port Hueneme, CA.
Result	:	The authors indicated that removal of DIPE was comparable to that achieved for MTBE, which was greater than 99.9%.
Test condition	:	Bioreactors (Autoclave Engineers, Erie, PA) were initially seeded with 2 L of mixed liquor from the MSD, 600 mL of mixed liquor from Shell Development Co., and 140 mL of aquifer wash water. Cultures were maintained on a total influent feed of 417 mg/L chemical oxygen demand (COD) divided as 50% methyl tert-butyl ether (MTBE) and 50% as diisopropyl ether (DIPE). Reactors were well mixed and controlled to a temperature of 20°C. To retain high biomass levels, a polyethylene porous pot was inserted into the reactor. The pots consisted of 0.45 cm thick filter-grade polyethylene (pore size = 20 mm), with an internal diameter of 19.1 cm and a height of 29.2 cm. Initially, a solids retention time of 18 days was maintained by wasting intentionally from the reactor. Subsequently (after about 120 days) intentional wasting ceased and only took place during sampling of the reactors. The combined influent flow rate was 2.37 L/d, with 80% of the total flow provided by a pH-adjustment solution, and 20% provided by an acidified nutrient solution. The pH-adjustment solutions contained deionized water, MTBE and DIPE fed by a syringe infusion pump, and an appropriate amount of 10N sodium hydroxide to maintain the pH between 7.4 and 8.0. The nutrient solution consisted of deionized water with essential salts and vitamins added to promote biological growth. Final nutrient concentrations inside the reactor were as follows: (NH4)2SO4, 93 mg/L; MgSO4, 69.6 mg/L; CaCl2o2H2O, 22.5 mg/L; K2HPO4, 6.9 mg/L; CuSO4oH2O, 0.08 mg/L; Na2MoO4o2H2O, 0.15 mg/L; MnSO4oH2O, 0.13 mg/L; ZnCl2, 0.23 mg/L; CoCl2o6H2O, 0.42 mg/L; and FeCl2o4H2O, 17.25 mg/L.. The hydraulic retention time was 4.2 days with a total reactor volume of 9.95 L and an enrichment culture volume of 6 L. Effluent from the reactors was monitored weekly for the presence of MTBE and DIPE using gas chromatography equipped with a flame ionization detector (FID) and a 60/80 Carbopack B5% Carbowax 20 M glass column. The pH of the system was measured daily, and COD and dissolved organic carbon (DOC) was measured weekly.
Conclusion	:	Diisopropyl ether can be effectively biodegraded in high biomass aerobic reactors.
Reliability	:	(2) valid with restrictions The report provided adequate details of the test conditions but reported only a text description of biodegradation results.

07.02.2006 (33)

Type	:	
Inoculum	:	other: soil and groundwater from a site previously exposed to methyl tert-butyl ether
Contact time	:	1 year
Degradation	:	(±) % after
Result	:	
Deg. product	:	
Method	:	other: (soil/water microcosm)
Year	:	1999
GLP	:	no
Test substance	:	other TS: diisopropyl ether (CAS No. 108-20-3)

Remark	:	Test type: soil/water microcosm
Result	:	No detectable biodegradation of the test substance occurred after one year of incubation.
Test condition	:	Soil and water from an aquifer with previous exposure to methyl tert-butyl ether (MTBE) was collected using a coring device and a pump. The material was brought to the laboratory where the sediment was thoroughly mixed. Groundwater was filtered through a 0.45 mm filter and sparged for 12 hours with sterile air to oxygenate the water and to remove background volatile chemicals. Analysis by gas chromatography indicated that concentrations of MTBE in the aqueous samples were <10 mg/L. Microcosms were constructed in amber 255-mL screw-top bottles sealed with TeflonÒ MininertÒ valves. Each bottle contained 150 g of wet sediment, 140 mL of sterile groundwater and 3000 mg/L of diisopropyl ether (DIPE). Treatments were constructed in triplicate with matching abiotic controls. Sediment used for the abiotic controls was autoclaved for one hour on each of three consecutive days. Additionally, 250 mg/L of mercuric chloride was added to ensure no biological activity. Microcosms were incubated in the dark at 16 °C. All samples were analyzed every 30 days by purge and trap gas chromatography and flame ionization detection to determine concentrations of the test substance. Test substance disappearance relative to abiotic controls was the principal indicator of biodegradation.
Conclusion	:	The test substance was not aerobically biodegraded by indigenous subsurface microflora.
Reliability	:	(2) valid with restrictions The testing method did not follow any specific regulatory guideline method, but the publication provided valuable information using sound scientific principles.

07.02.2006 (47)

Type	:	anaerobic
Inoculum	:	other: sediment and groundwater from an anoxic aquifer polluted by municipal landfill leachate
Contact time	:	252 day(s)
Degradation	:	(±) % after
Result	:	
Deg. product	:	
Method	:	other: (closed serum bottle test)
Year	:	1993
GLP	:	no
Test substance	:	other TS: diisopropyl ether (CAS No. 108-20-3)
Result	:	Biodegradation Rate (ppm C/day) = 0 Methane recovery (% theoretical) = 0
Test condition	:	Diisopropyl ether was tested for the ability of the compound to be completely biodegraded to methane in an aquifer slurry. Sediment and groundwater were collected from a methanogenic portion of a shallow anoxic aquifer polluted by municipal landfill leachate. Slurries were prepared by placing 50 g of sediment and 75 mL of groundwater in sterile 160-mL serum bottles. The bottles were sealed with Teflon-lined stoppers and incubated in the dark at room temperature. Diisopropyl ether was added to the incubation mixture to reach an initial substrate concentration of 50 ppm C. Pressure increases resulting from biogas formation (CH4 and CO2) were monitored with an automated pressure transducer system. The acclimation time was estimated as the amount of time where no significant pressure difference was measured between the substrate-amended treatment and un-amended controls. At the end of the incubation period, biodegradation was measured as the depletion of parent substrate and the formation of methane over background controls. Measurements were made using gas

chromatography equipped with a flame ionization detector. A 1.8 m x 0.32 cm 80/100 porapak Q column or a 0.2% Carbowax 1500 on Carbopack C column were used for headspace methane analyses and test substance determinations, respectively. Autoclaved controls were similarly assayed and were uniformly unable to exhibit methane formation or test substance disappearance. The amount of methane formed in aquifer incubations was compared to that theoretically expected based on the Buswell equation.

Conclusion : Diisopropyl ether was a persistent molecule that resisted anaerobic destruction. After 252 days, no evidence for the anaerobic biodegradability of diisopropyl ether was obtained.

Reliability : (2) valid with restrictions
The publication reported a well-documented study that meets basic scientific principles.

07.02.2006 (43)

Type : anaerobic
Inoculum : other: Sediment and surface or groundwater
Deg. product :
Method : other: unknown
Year : 1994
GLP : no
Test substance : other TS: diisopropyl ether (CAS No. 108-20-3)

Remark : Exposure period: 85, 180, or 244 days
Result : Biodegradation of diisopropyl ether with sulfate or nitrate available as electron acceptors:

	SO4 or NO3 Substrate Loss (%)	Amount Consumed (% Theoretical)	Rate (umol/SO4/day)
sulfate-reducing	0	0	0
nitrate-reducing	0	0	0

Biodegradation of diisopropyl ether under methanogenic conditions:

	Degradation Rate (ppm C/day)	Methane Recovery (% Expected)
Fuel-impacted river sediment	0	0
Industrial/sewage impacted creek sediment	0	6

Test condition : Several tests were carried out to determine the anaerobic biodegradation of the test substance. Three experiments were done to determine biodegradation under sulfate- and nitrate-reducing conditions and under methanogenic conditions. Sediment and surface water (or groundwater) from three sources were used as inoculum in separate experiments; (1) sediment/groundwater from a landfill leachate impacted aquifer, (2) sediment/surface water from a river historically impacted by oil storage and barge loading facilities, and (3) sediment/surface water from a creek impacted by industrial waste and domestic sewage sludge.

Slurries were prepared by placing 50 g of sediment and 75 mL of water into sterile 160-mL serum bottles. Water was amended with sodium sulfide (1 mM) and resazurin (0.0002%) to serve as reductant and redox indicator, respectively. The bottles were sealed with stoppers and the headspace above the slurries was adjusted to 80% N2:20%CO2 (1 atm). To the landfill leachate-impacted samples, either sodium sulfate (5mM) or sodium nitrate (8 mM) was added in order to assess potential test substance decay coupled with the consumption of these electrons (referred to as sulfate-reducing and nitrate-reducing incubations, respectively). The test substance was added to the slurries to give an initial concentration of 50 ppm C. The rates of methane production, sulfate reduction, and nitrate

depletion were monitored in slurries receiving the test substance and compared to test substance-free controls. All incubations were done in the dark at 24°C. The sulfate-reducing experiment was run for 244 days, the nitrate-reducing experiment was run for 85 days, and the methanogenic experiment was run for 180 days.

In the methanogenic incubations, increases in headspace pressure were routinely monitored. Parent compound depletion and formation of methane were confirmed by gas chromatography (GC). The net amount of sulfate and nitrate depletion over the controls was monitored by high pressure liquid chromatrography (HPLC).

Conclusion : Diisopropyl ether is not anaerobically degraded under nitrate- or sulfate-reducing conditions, and it is not anaerobically degraded under methanogenic conditions.

Reliability : (2) valid with restrictions
The publication reported a well-documented study that meets basic scientific principles.

24.02.2006 (32)

Type : aerobic
Inoculum : other: Gordonia terrae strain IFP 2001 (CNCM Registration No. CTP 1-1889); isolated from activated sludge taken at an urban waste water treatment plant
Contact time : 24 hour(s)
Degradation : (±) % after
Result :
Deg. product :
Method : other: (sealed flasks, shaken)
Year : 2000
GLP : no
Test substance : other TS: diisopropyl ether (CAS No. 108-20-3)

Result : Diisopropyl ether was degraded by 78% over the 24-hour incubation period.

Comparison of DIPE biodegradation to ETBE:

Test Substance	Degradation (%)
ETBE	100

The authors indicated concentrations of the test substance in the flasks were quantified by analytical means. The method was not described in the report, but was referenced in an earlier publication by the same workers.

Test condition : The capacity of ethyl t-butyl ether (ETBE)-induced resting cells of the inoculum to degrade diisopropyl ether was tested in sealed flasks. The article focused on biodegradation of ETBE, methyl t-butyl ether (MTBE) and t-amyl methyl ether (TAME), but was tested on other ethers including diisopropyl ether (DIPE).

G. terrae IFP 2001 was cultivated on ETBE-supplemented MM medium. After 24 hours incubation, bacteria were harvested by centrifugation (20,000 g for 20 minutes), washed twice in 100 mM Tris-HCl buffer at pH 7.0 and re-suspended in Tris-HCl. The test substance was added to 20-mL cell suspensions in 125-mL sealed flasks. Flasks were incubated for 24 hours at 30 °C with orbital shaking. Initial cell concentration was 0.5 g/L. The test substance was tested at 100 mg/L. Filtered samples were analyzed at 0-hour and 24-hours.

Conclusion : Diisopropyl ether was degraded by 78% within 24 hours.

Reliability : (2) valid with restrictions
Information on the analytical method was not provided in the report.

07.02.2006 (21)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species	:	other: see remark
Exposure period	:	at 25 °C
Concentration	:	
BCF	:	= 2.95
Elimination	:	
Method	:	other: calculation
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl Ether (CAS # 108-20-3)
Remark	:	A log bioconcentration factor (BCF) of 0.47 is calculated (BCF = 2.95). With respect to a log Kow = 1.52, which was used to calculate the BCF, diisopropyl ether in the aquatic environment is expected to have a low bioaccumulation potential.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag	:	Critical study for SIDS endpoint

12.12.2005 (14)

Species	:	other: see remark
Exposure period	:	at 25 °C
Concentration	:	
BCF	:	= 14.06
Elimination	:	
Method	:	other: calculation
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)
Remark	:	A log bioconcentration factor (BCF) of 1.15 is calculated (BCF = 14.06). With respect to a log Kow = 2.4, which was used to calculate the BCF, disiopropyl ether in the aquatic environment is expected to have a low bioaccumulation potential.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated and not measured.

12.12.2005 (14)

3.8 ADDITIONAL REMARKS

Memo	:	Biodegradation of diisopropyl ether
Remark	:	The article reports on a U.S EPA and American Petroleum Institute workshop (February 1-3, 2000) on biodegradation of methyl tert-butyl ether (MTBE)-contaminated soils and groundwater. MTBE is one of a group of structurally similar compounds commonly called alkyl ether oxygenates (AEO) that are added to reformulated gasoline to reduce carbon monoxide and ozone emissions. Diisopropyl ether (DIPE) is one type of AEO that is used in gasoline along others in this class of chemicals. The workshop focused on the status of the current research and understanding on biodegradation of MTBE and reported relevant information on the biodegradation of DIPE and other AEOs used in reformulated gasoline.

Pure microbial cultures have been identified and isolated that have demonstrated the capability of utilizing MTBE as a sole carbon and energy source under aerobic conditions (Scow et al., 2000). This isolate, bacterial strain PM1, was studied by Church and Tratnyek (2000) to determine the aerobic degradation pathway of MTBE. In their study, the authors confirmed the mineralization of MTBE and determined the degradation rates of DIPE and other AEOs were of the same order of magnitude as the degradation rates of MTBE (Church and Tratnyek, 2000). Their results suggested that similar enzyme systems were responsible for all of the reactions.

While the majority of research on anaerobic biodegradation of these compounds has been unable to show that MTBE is utilized, a few studies have demonstrated that MTBE and other AEOs may be susceptible to attack under anaerobic conditions. Kropp et al. (2000) studied the anaerobic biodegradation potential of MTBE, DIPE, and other oxygenates in sediment slurries under methanogenic conditions. They found definite evidence in the form of methane and carbon dioxide production to conclude that anaerobic degradation was occurring. The workshop authors concluded that anaerobic biodegradation was a phenomena that was not widespread and extremely difficult for these compounds.

07.02.2006 (7) (12) (24) (36)

Memo : Biodegradation of diisopropyl ether under aerobic and anaerobic conditions - summary

Remark : Diisopropyl ether (DIPE) is one of a group of similar compounds referred to as alkyl ether oxygenates (AEO) that are added to reformulated gasoline. Biodegradation studies with DIPE and other AEO compounds have demonstrated the ability of these substances to be consumed by pure strains and mixed cultures of bacteria when incubated under aerobic conditions. Church and Tratnyek (2000) showed that bacterial strain PM1, which had been acclimated to methyl t-butyl ether (MTBE), could mineralize MTBE and demonstrated similar degradation rates for DIPE and other AEOs. They concluded that similar enzymes were responsible for all the degradation reactions. Additional evidence showing the wide spectrum of activity of the bacterial enzyme systems to degrade AEOs was provided by Hernandez-Perez et al. (2001). Using isolated Gordonia terrae (strain IFP 2001) that had been grown on ethyl t-butyl ether (ETBE), degradation of a variety of other AEOs could be achieved. DIPE was degraded 78% within 24 hours in their study (Hernandez-Perez et al. 2001).

Optimum biodegradation in mixed culture systems occurred when the microbial culture is allowed a period of acclimation to the substrate. For example, Bridié et al. (1979) measured only 7% consumption of the theoretical oxygen demand when DIPE was tested in a 5-day BOD test. In contrast, Cano et al. (1999) showed rapid utilization of DIPE when activated sludge was conditioned to a cocktail of volatile organic compounds for two months. In a continuous flow reactor, DIPE removal averaged 99.4%. Cano et al. (1999) also measured high rates of biodegradation of DIPE when comparing the continuous treatment method (EPA Method 304B) (EPA, 1994) to two batch treatment methods (BOX and SBT methods; Rajagopalan et al., 1998). Based on the measured rate constants, the authors considered DIPE to be readily biodegradable. Pruden et al. (2001) also observed high removal rates (e.g., 99.9%) of DIPE through a continuous flow reactor system. The performance of the reactors was enhanced when biomass was retained in the reactor, suggesting that a long biomass residence time may be needed for complete mineralization.

Biodegradation of DIPE is not always observed in biodegradation assays.

Zenker et al. (1999) failed to show biodegradation of DIPE over a 1-year period using indigenous microflora in sediment and water from an aquifer that had been previously exposed to MTBE. Given the apparent need of microbial communities for a period of acclimation to DIPE, it is unlikely that DIPE would be considered readily biodegradable in standard guideline studies. However, the evidence shows that DIPE can be inherently degraded by pure strains of bacteria and mixed enrichments of activated sludge microorganisms.

While available research shows that DIPE is capable of being biodegraded under aerobic conditions, anaerobic biodegradation is extremely difficult and this substance is considered recalcitrant under those conditions. Suflita et al. (1993) showed no biodegradation of DIPE after 252 days of anaerobic incubation. Substrate was added as 50 ppm C to sediment and groundwater collected from a methanogenic portion of a shallow anoxic aquifer. Similarly, DIPE was evaluated for anaerobic biodegradability under methanogenic conditions as well as sulfate and nitrate-reducing conditions (Mormile et al., 1994). Inocula from three sources (e.g., sediment/groundwater from an aquifer impacted by landfill leachate, sediment/surface water from a river impacted by oil storage, and sediment/surface water from a creek impacted by industrial waste and domestic sewage) were used in separate incubations to assess anaerobic biodegradation in sealed serum bottles. No DIPE biodegradation was measured over incubation periods of 85 days (nitrate-reducing conditions), 180 days (methanogenic conditions), and 244 days (sulfate-reducing conditions). Lack of methane production reported by Suflita and Mormile (1993) does not preclude partial anaerobic biodegradation of DIPE in their studies because only methane was monitored. Kropp et al. (2000) studied the anaerobic biodegradation potential of a number of AEOs including DIPE in sediment slurries under methanogenic conditions. They found evidence in the form of methane and carbon dioxide production to conclude that anaerobic biodegradation was occurring, although the authors stated that anaerobic biodegradation was not a widespread phenomena and extremely difficult for these compounds.

27.02.2006

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 91.7
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Flow-through Fish Acute Toxicity Test
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)
Method	:	The water solubility of the test chemical was obtained from literature or determined experimentally. A flow through system using proportional diluters and modified continuous mini-diluter system was used for maintaining the required test concentrations Twenty to twenty-five 30 day-old fish, each weighing approximately 0.12 g, were randomly divided amongst the test tanks (control and five different concentrations) with flow-through dilutor systems. Lake Superior water maintained at 25°C ± 1°C was used in the test. Routine measures of hardness (EDTA) and total alkalinity of test water yielded mean values of 45.5 and 42.2 mg/L as CaCO3, respectively. The arithmetic mean of the pH was 7.5 and dissolved oxygen was always greater than 60% of saturation. Fish were supplied from the United States Environmental Protection Agency, Environmental Research Laboratory-Duluth culture. They were not fed during the test. Deaths were recorded after 1, 3, 6,12, 24, 48, 72, and 96 hours.
Remark	:	Statistics: Trimmed Spearman-Karber Method Test method described in reference.
Result	:	96-hour LL50 = 91.7 mg/L based upon measured values Analytical method used was GC analysis with Flame Ionization Detection (GC-FID), performed on a Hewlett-Packard model 5730A gas chromatograph. Concentrations of the test chemical were measured daily at each exposure level.
Conclusion	:	96-hour LC50 = 91.7 mg/L based upon measured values.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because complete information on the analytical results were not available and the study was not conducted under GLP.
Flag	:	Critical study for SIDS endpoint

01.11.2005 (45)

Type	:	
Species	:	other: Fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 214.1
Method	:	other: ECOSAR version 0.99h, US EPA
Year	:	
GLP	:	
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method	:	ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound. To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish 96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach.
Result	:	LC50, 96 h, for fish = 214.1 mg/L
Test condition	:	Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program. Class: Neutral organics
Test substance	:	Diisopropyl Ether (CAS No. 108-20-3)
Conclusion	:	The predicted 96 h LC50 value for fish (214.1 mg/L) is in good agreement with the experimental 96 h LC50 value for fathead minnow (Pimephales promelas) (91.7 mg/L) (Veith et al., Can. J. Fish. Aquat. Sci., 40:743-748) and 48 h EC50 value for Daphnia (190.0 mg/L) (Stephenson R.R., Shell Research Limited, Report No. SBGR.83.215).
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated and not measured.

28.10.2005 (13)

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 786
EC50	:	= 476
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Flow-through Fish Acute Toxicity Test
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method	:	Test solutions were prepared using a proportional diluter system without replication. This system provided control and five test substance concentrations to glass test vessels. Each vessel held 2 L of test solution and the diluter flow rate was sufficient to provide 18 volume additions per day. An aqueous stock solution of 1050 mg/L was used by the diluter to

prepare the exposure series. Dilution water was filtered Lake Superior water. Typical ranges of water quality factors measured in this water were pH (7.4 - 8.2), total hardness (44 - 53 mg/L as CaCO3), and specific conductance (78 - 86 mmhos/cm).

Test fish originated from in-house cultures of P. promelas at the U.S. EPA Environmental Research Laboratory - Duluth. Fish were not fed 24 h prior to testing or during the test. At test initiation, fish were randomly placed in test vessels until each vessel contained 10 individuals. Individuals used in testing were 34 d old and measured 19.0 mm mean length (SD = 2.534) and 0.104 g mean weight (SD = 0.0433). Biomass loading was 1.04 g/L. Death was the major test endpoint. Numbers of dead fish were counted daily and any dead fish were removed from the vessels. Abnormal behavioral changes were recorded at each observation time. LC50 (lethality) and EC50 (total effect) values were determined.

Temperature, dissolved oxygen, and pH were measured daily in all test chambers. Mean values (and Standard Deviation) were 24.9 °C (SD = 0.52), 7.3 mg/L (SD = 0.13), and 7.75 (SD = 0.16), respectively. Total hardness and alkalinity were measured once in the control, low, medium, and high test levels. Mean values were 43.7 mg/L total hardness as CaCO3 (SD = 0.96) and 49.6 mg/L alkalinity as CaCO3 (SD = 0.25). Lighting was provided by fluorescent bulbs that produced 28 to 48 lumens/sq ft at the water surface. The photoperiod was 16 h light and 8 h dark.

Test substance concentrations were verified in most cases daily during the test using gas-liquid chromatography. Concentrations were averaged and a mean percent recovery was calculated. The nominal with measured concentrations in parentheses were, control (not detected), 157 mg/L (131 mg/L), 242 mg/L (210 mg/L), 373 mg/L (382 mg/L), 574 mg/L (594 mg/L), and 883 mg/L (1044 mg/L). The overall percent recovery was 98.7%.

Remark : Statistics: LC/EC50 values determined by Trimmed Spearman-Karber Method

Result : 96-hour LC50 = 786 mg/L based on mean measured values.
96-hour EC50 = 476 mg/L based on mean measured values.

The EC50 value was based on mortality and the following abnormal effects: loss of schooling behavior, swimming near the surface, hypoactive, under-reactive to external stimuli, loss of equilibrium.

Conclusion : 96-hour LC50 = 786 mg/L based on mean measured values.
96-hour EC50 = 476 mg/L based on mean measured values.

Reliability : (1) valid without restriction
12.12.2005 (16)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 900
Limit test :
Analytical monitoring : yes
Method : other: Flow-through Fish Acute Toxicity Test (ASTM, 1980)
Year : 1985
GLP : no data
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : Test solutions were prepared using a continuous-flow diluter delivery system, which delivered four test substance concentrations and control solutions to duplicate test vessels. Dilution water was filtered Lake Superior water. Average values for water quality factors for the dilution water were: hardness (44.6 mg/L as CaCO3), total alkalinity (44.0 mg/L as

CaCO3), and pH (7.6). Test chambers were glass vessels and contained 2 L of test solution. Solution flow rates through the test chambers was sufficient to provided at least a 95% replacement in approximately 4 h. Test substance concentrations were verified daily during the test using either gas chromatography or high pressure liquid chromatography methods.

The mean temperature for the test was 25 ± 0.5°C, and dissolved oxygen remained at or above 80% saturation. Lighting was provided by wide spectrum fluorescent bulbs at an intensity of 22 to 38 lumens/sq ft over the test chambers. The photoperiod was 16 h light and 8 h dark with a 30-min dusk/dawn transition period.

Test fish originated from cultures maintained by the U.S. EPA Environmental Research Laboratory - Duluth, MN. and were 28 to 34 days old (weighing approximately 0.12 g) at the time of testing. A total of 20 fish per treatment (10/replicate) was used in the test. Fish were added to the test chambers 2-3 h before introduction of the test solutions. Fish were not fed 24 h before or during the test. Mortalities were recorded daily.

Remark : Statistics: Trimmed Spearman-Karber Method or log-probit method.
Result : 96-h LC50 = 900 mg/L based on measured concentrations
95% CL = 881 - 920 mg/L
Conclusion : 96-h LC50 = 900 mg/L based on measured concentrations
Reliability : (1) valid without restriction
12.12.2005 (3)

Type : static
Species : Carassius auratus (Fish, fresh water)
Exposure period : 24 hour(s)
Unit : mg/l
LC50 : = 380
Limit test :
Analytical monitoring : yes
Method : other: static acute fish toxicity test (APHA, 1971)
Year :
GLP : no data
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : The test consisted of exposing groups of six fish to a series of concentrations of the test substance for 24 h. Fish were exposed in an all glass tanks holding 25 liters of test solution. Dilution water was local tap water having the following characteristics (all values in mg/L): Cl^{-} = 65; $NO2^{-}$ = 0; $NO3^{-}$ = 4; $SO4^{-}2$ = 35; $PO4^{-}3$ = 0.15; $HCO3^{-}$ = 25; SiO2 = 25; NH4+ = 0; Fe = 0.05; Mn = 0; Ca+2 = 100; Mg+2 = 8; alkali as Na+ = 30; pH = 7.8.

The test was run at a temperature of 20±1°C, and the solutions were not aerated during the test period.

Test fish had a mean length of 6.2±0.7 cm, a mean weight of 3.3 ± 1.0 g and were in good health at the time of testing.

Exposure concentrations were confirmed either by total organic carbon analysis or by extraction and subsequent analysis by gas chromatography. Measured concentrations were not reported in this study.

Remark : Determination of LC50 by graphical interpolation of log concentrations versus percent mortality (APHA, 1971).
Result : 24-hour LC50 = 380 mg/L

The analytical method was either total organic carbon analysis or gas chromatography. It was not reported what method was employed for this test substance nor if the result was based on measured concentrations.

Conclusion	:	24-hour LC50 = 380 mg/L.
Reliability	:	(3) invalid The test was run for only 24 hours to ensure that the dissolved oxygen content did not fall below 4 mg/L. The report lacked sufficient detail for assessment. It was not stated whether results were based on nominal or measured values.

12.12.2005 (1)

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	7000
Limit test	:	
Analytical monitoring	:	no
Method	:	other: static acute fish toxicity test
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method :

The test consisted of exposing groups of fish to a four-dilution series of the test substance for a period of 96 h. Test vessels were all glass 5-gallon aquaria. The volume of test solution was adjusted to assure that a biomass loading was no more than 1 g fish /liter solution. Dilution water was well water having a typical pH of 7.6 to 7.9 and a hardness of 55 mg/L (as CaCO3).

Fish were obtained from a commercial source and assessed for health during a 14-d acclimation period prior to testing. During that time they were maintained on a commercial fish food diet supplemented with minced frozen shrimp. Fish were not fed 48 hours prior to testing. Fish were randomly selected for testing and were approximately 33 to 75 mm in length.

The test was run at 23°C. Test solutions were not aerated for the initial 24 h, but aeration was applied thereafter if the dissolved oxygen concentration was being depleted. Dissolved oxygen readings were taken daily, and pH was measured at the end of the test. However, these data were not provided in the report.

Mortality was assessed daily and any dead fish were removed at each observation time.

Remark	:	The LC50 was determined by plotting survival percentages on semi-logarithmic paper and drawing a straight line fit through or near significant points above and below 50% survival.
Result	:	96-hour LC50 = 7,000 mg/L The mortality pattern reported for the test substance suggests that a more likely estimate of the LC50 value would lie between 7,900 and 10,000 mg/L, rather than 7,000 mg/L. This was due to a non-monotonic dose response pattern of mortality. The report authors indicated that the LC50 value was higher than the published solubility for the test substance.
Conclusion	:	96-hour LC50 = 7,000 mg/L based on nominal concentrations
Reliability	:	(3) invalid Documentation was insufficient for evaluation. Basic water quality data during the test were not provided. The authors stated that aeration of the test solutions was used after 24 hours to ensure maintenance of dissolved oxygen. No analytical verification of exposure concentrations were made.

12.12.2005 (10)

Type	:	static
Species	:	Menidia beryllina (Fish, estuary, marine)

Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	6600
Limit test	:	
Analytical monitoring	:	no
Method	:	other: static acute fish toxicity test
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : The test consisted of exposing groups of fish to a four-dilution series of the test substance for a period of 96 h. Test vessels were all glass 5-gallon aquaria. The volume of test solution was adjusted to assure that a biomass loading was no more than 1 g fish /liter solution. Dilution water was prepared by adding "instant ocean" salts to well water (pH of 7.6 to 7.9; hardness 55 mg/L (as CaCO3)) until a specific gravity of 1.018 was achieved.

Fish were field collected in nets from Horseshoe Bay at Sandy Hook, New Jersey. They were held for a 14-d acclimation period prior to testing and assessed for health during that time. During the acclimation period they were fed minced frozen shrimp. Fish were not fed 48 hours prior to testing. Fish were randomly selected for testing and were approximately 40 to 100 mm in length.

The test was run at 20°C, and test solutions were continuously aerated during the exposure period. Dissolved oxygen readings were taken daily, and pH was measured at the end of the test. However, these data were not provided in the report.

Mortality was assessed daily and any dead fish were removed at each observation time.

Remark : LC50 determined by graphical interpolation of the logarithm of the concentration versus the percentage mortality.

Result : 96-hour LC50 = 6600 mg/L

The mortality pattern reported for the test substance does not correspond with the estimated LC50 value. Given the dose-response pattern, the LC50 value would lie between 3,200 and 5,000 mg/L, rather than 6,600 mg/L. The authors reported that the result was higher than the reported water solubility of the test substance.

Conclusion : 96-hour LC50 = 6600 mg/L based on nominal concentrations.

Reliability : (3) invalid
Documentation was insufficient for evaluation. Basic water quality data during the test were not provided. The authors stated that aeration of the test solutions was used after 24 hours to ensure maintenance of dissolved oxygen. No analytical verification of exposure concentrations were made.

12.12.2005 (10)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 190
Analytical monitoring	:	no
Method	:	other: U.S. Environmental Protection Agency, Methods for acute toxicity testing with fish, macro-invertebrates and amphibians (EPA-660/3-75-009)
Year	:	1975

GLP : no
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Remark : Statistics:
Probit analysis after log transformation of the concentrations (Finney, 1971)
Probit Analysis, Finney, D.J., Cambridge University Press, 3rd edition, p333 (1971)

Result : The 24 h and 48 h Effect Concentration (EC50) values were calculated to be 240 mg/L (95% fiducial limits 210 to 280 mg/L) and 190 mg/L (95% fiducial limits 160 to 220 mg/L), respectively.
The immobilization (%) of Daphnia magna (n=10/replicate) are as follows:

Test Substance Loading Rate (mg/L)	Immobilization (%)* 24 hr	48 hr
0 (control)	0	0
46	0	0
99	3	7
210	27	57
460	100	100
1000	100	100

*mean of 3 replicates

Test condition : A 48 hour static toxicity test was carried out without renewal of the test solutions. Quantities of stock solutions of di-isopropyl ether in acetone were added in triplicate sets of 110 mL glass flasks so that when made up with reconstituted freshwater, an approximately logarithmic series of concentrations ranging from 46 to 1000 mg/L was produced. Three flasks served as controls and received no test substance. The concentration of acetone in all control and test flasks was 0.1 mL/L. Precautions were taken to (a) minimise evaporative loss of the test substance by use of glass cover slips over the vessel necks and (b) to minimize the risk of organisms becoming trapped at the surface by placing black paper caps over the flasks to create a darkened zone which the organisms would avoid.
The test temperatures were in the range 20 ± 2°C, pH was in the range 8.2 to 8.4, the total hardness was 164 mg/L as CaCO3, and dissolved oxygen was in the range 8.2 to 9.2 mg/L.
The daphnids were cultured in-house, derived from a strain obtained (via ICI Brixham Laboratory) from Institut National de Recherche Chimique Applique (I.R.Ch.A.), France. Age was <24 hours old from 15 to 35 day old parents.
All concentrations of test substance are expressed in terms of quantities initially added to the test vessels.

Test substance : Diisopropyl Ether (CAS No. 108-20-3)
Conclusion : After Daphnia magna were exposed to test solutions of di-isopropyl ether for 48 hours in a static test, the 24 h and 48 h EC50 values were calculated to be 240 mg/L and 190 mg/L, respectively.
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because it did not analytically verify exposure concentrations and the results are based on nominal values.

07.12.2005 (40)

Type :
Species : other: Daphnia
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 221.9
Method : other: ECOSAR version 0.99h, US EPA
Year :
GLP :
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method	:	ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound. To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish 96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach.
Result	:	EC50, 48 h, for Daphnia = 221.9 mg/L
Test condition	:	Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program. Class: Neutral organics
Test substance	:	Diisopropyl Ether, CAS No. 108-20-3
Conclusion	:	The predicted 48 h LC50 value for Daphnia (221.9 mg/L) is in close agreement with the experimental 48 h EC50 value for Daphnia (190.0 mg/L) (Stephenson R.R., Shell Research Limited, Report No. SBGR.83.215).
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated and not measured.

28.10.2005 (13)

Type	:	other: Daphnid acute immobilization test
Species	:	other: Daphnia magna Straus
Exposure period	:	48 hour(s)
Unit	:	
Analytical monitoring	:	yes
Method	:	other: OECD Guideline 202, USEPA OPPTS 850.1010
Year	:	
GLP	:	yes
Test substance	:	other TS: Diisopropylether (CAS No. 108-20-3)
Method	:	Statistical Method: The EC50 and 95% confidence limits were calculated using the Trimmed Spearman-Karber method. The NOEC was determined using a Fisher's exact test. A Hochberg adjustment was used to control the experiment-wise error rate for the Fisher's test at the same alpha level. All statistical analyses were performed with SAS for Windows.
Remark	:	Year (guideline): 2004 (OECD), 1996 (USEPA) Year (study performed): 2007

Result	:	Control survival was 100% at 48 hours. After 48 hours, immobility was 0, 0, 0, 10, 75, and 100% in the control, 74.4, 135, 280, 498, and 1,060 mg a.i./L treatments. After 24 hours, 15 daphnids were observed to be quiescent (able to weakly swim within 15 seconds of gentle agitation) in the 498 mg a.i./L test treatment. Sixteen daphnids in the 280 mg a.i./L test treatment and five daphnids in the 498 mg a.i./L test treatment were observed to be quiescent after 48 hours. The 24-hour EC50 based on immobility, sublethal effects, and mean measured concentrations was estimated to be 350 mg a.i./L with 95% confidence limits of 320 to 382 mg a.i./L. The 48-hour EC50, based on immobility, sublethal effects, and mean measured concentrations, was estimated to be 208 mg a.i./L with 95% confidence limits of 190 to 227 mg a.i./L. The 48-hour NOEC was 135 mg a.i./L based upon the lack of statistically significant immobility and sublethal effects at this and all lower concentrations. Measured DIPE concentrations at 0-hour were <MQL, 79.1, 148, 290, 541, and 1,130 mg a.i./L or 108 to 126% of the nominal concentrations. DIPE concentrations at 24 hours in the old solutions were <MQL, 71.5, 134, 255, 343, and 935 mg a.i./L or 69 to 113% of the nominal concentrations. DIPE concentrations at 24 hours in the new solutions were <MQL, 76.8, 148, 290, 562, and 1,110 mg a.i./L or 111 to 122% of the nominal concentrations. DIPE concentrations at 48 hours in the old solutions were <MQL, 70.1, 109, 286, and 544 mg a.i./L or 87 to 114% of the nominal concentrations. Level five was not analyzed due to 100% immobility after 24 hours. Mean measured concentrations of DIPE were <MQL (control) 74.4, 135, 280, 498, and 1,060 mg a.i./L or 100 to 118% of the nominal concentrations.
Source	:	IPA Panel, American Chemistry Council
Test condition	:	Test solutions were prepared on a volume to volume basis by direct addition of the test substance to 1.8L of dilution water. Test solutions were corrected for purity and density of the test substance. Treated test solutions were prepared by addition of 0.157, 0.312, 0.624, 1.25, and 2.50 mL of DIPE to 1.8L of dilution water resulting in nominal concentrations of 63, 125, 250, 500, and 1,000 mg a.i./L. The control solution consisted of dilution water only. Dilution water was an aged laboratory freshwater prepared by blending naturally hard well water with well water that was demineralized by reverse osmosis. These waters were blended to yield a total hardness of 130 to 160 mg CaCO3/L and biologically aged. The water was filtered through a sediment filter and UV irradiated prior to use. Total alkalinity and total hardness of the dilution water at test initiation were 142 and 142 mg CaCO3/L, respectively. Conductivity of the dilution water was 343 µS. Test chambers were 250-mL glass jars filled so that there was minimal headspace. Test chambers were covered with a glass plate to reduce volatilization of test substance. The control and test substance treatments were tested in quadruplicate. Five water fleas were distributed to each replicate for a total of 20 water fleas per treatment. Observations for immobility and sublethal responses (e.g., discoloration, lethargy, etc.) were made once every 24 hours (± 1 hour from initiation). Test chambers were maintained at 20 ± 1°C in a temperature-controlled water bath. Fluorescent lighting was maintained on a 16-hour daylight photoperiod with two 30-minute simulated dawn and dusk periods. Test solutions were renewed at 24 hours. Daphnia magna neonates (<24-hours old) were obtained from an in-house daphnid culture. All daphnids were cultured in a temperature-controlled area at approximately 20°C. During the holding period, the daphnids were fed a suspension of the algal species Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum) at least once a day supplemented by an artificial diet. One day prior to neonate selection, the adult daphnids were isolated, by transferring the adults to a fresh culture with a water/food suspension. The adults were considered acceptable with no visible signs of

stress, disease or physical damage. No adult immobility occurred during the 48-hour period immediately prior to production of neonates used in test initiation. Daphnids were not fed during the test.

Test solution temperatures during the 48-hour exposure ranged from 20.2 to 20.9°C. Light intensity during the definitive test was approximately 382 lux. Dissolved oxygen concentrations in the new solutions ranged from 7.9 to 8.6 mg/L (92 to 101% saturation) and from 7.4 to 8.2 mg/L (85 to 94% saturation) in the old solutions. Test solution pH ranged from 8.2 to 8.5. The control and all test substance treatments appeared clear and colorless throughout the test with no visible precipitates, surface films, or undissolved test substance.

Concentrations of DIPE were measured by gas chromatography (GC) using a flame ionization detector (FID). Sample analysis was performed using a purge and trap autosampler and sample concentrator. The minimum quantifiable limit (MQL) was 0.404 mg a.i./L. Recoveries from quality control fortifications ranged from 90 to 134 % of the nominal concentrations. Ten-milliliter samples were collected from new parent solutions at test initiation (0 hour) and solution renewal (24 hours) and composites from each replicate of the old solutions at 24 and 48 hours.

Conclusion : The 24-hour EC50 was 350 mg a.i./L with 95% confidence limits of 320 to 382 mg a.i./L. The 48-hour EC50 was 208 mg a.i./L with 95% confidence limits of 190 to 227 mg a.i./L. The 48-hour NOEC was 135 mg a.i./L.

Reliability : (1) valid without restriction

02.02.2008 (37)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: Green Alga
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	= 134.9
ChV	:	= 10.2
Method	:	other: ECOSAR version 0.99h, US EPA
Year	:	
GLP	:	
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound.

To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish

96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach.

Result : EC50, 96 h, for green algae = 134.9 mg/L

ChV, 96 h, for green algae = 10.2 mg/L

Test condition : Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program.
Class: Neutral organics

Test substance : Diisopropyl Ether (CAS No. 108-20-3)

Conclusion : The predicted 96 h EC50 value for algae (134.9 mg/L) is in the same range as the predicted 48 h LC50 value for Daphnia (221.9 mg/L) and the predicted 96 h LC50 value for fish (214.1 mg/L). There is also good comparison between the predicted and experimental EC50 values for Daphnia (221.9 mg/l v 190.0 mg/L, respectively) and for fish (214.1 mg/l v 91.7 mg/L, respectively).

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated and not measured.

28.10.2005 (13)

Species : Selenastrum capricornutum (Algae)
Endpoint : biomass
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : >= 1000
Limit test :
Analytical monitoring : no
Method : other: algae growth inhibition
Year : 1983
GLP : no data
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : A 4 d algal growth study was carried out using 10 concentrations of the test substance and a control. The test design included six control replicates and single vessels dosed with different concentrations of the test substance. 250-mL glass Erlenmeyer flasks served as the test vessels and held 50 mL of culture medium. Culture medium was prepare following the recipe given by Miller and Green (1978) with the following exceptions; 1) boric acid concentration = 105 mg/L, and 2) sodium bicarbonate concentration = 50 mg/L.

To 10 flasks, quantities of a test substance stock solution made up in acetone were added to give a logarithmic series of concentrations ranging from 1 to 1000 mg/L (1.0, 2.2, 4.6, 10, 22, 46, 100, 220, 460, and 1000 mg/L). The concentration of acetone in all flasks including controls was adjusted to 0.1 mL/L. Each flask was inoculated with S. capricornutum to give an initial cell density of 5 x 102 cells/mL. The algal inoculum was prepared from an actively growing liquid culture of S. capricornutum in exponential growth phase.

Flasks were incubated in a temperature controlled orbital incubator under constant illumination (approximately 3000 lux) at 24±2°C for 4 days. Cell counts were made on days 2 and 4 using an electronic particle counter (Coulter counter). The temperature in the incubator was measured at 4-h intervals. The pH of the control and highest test concentration was

measured on days 0, 2, and 4. Temperature remained within the 24±2°C specified range, and the pH ranged from 8.3 to 8.5 in the measured vessels.

All determination of EC50 values were based on nominal test concentrations and cell counts.

Result : 96-hour EC50 = >1000 mg/L based on nominal concentrations.

The 96-hour cell counts in the treated flasks as a percent of the mean control cell counts were:

1.0 mg/L = 84%	46 mg/L = 127%
2.2 mg/L = 108%	100 mg/L = 130%
4.6 mg/L = 91%	220 mg/L = 113%
10 mg/L = 122%	460 mg/L = 127%
22 mg/L = 129%	1000 mg/L = 91%

Conclusion : 96-hour EC50 = >1000 mg/L based on nominal concentrations.
Reliability : (3) invalid
Test concentrations were not measured and there is no indication in the report whether the test vessels were sealed. The reported LC50 value may reflect a loss of test substance by volatilization if the flasks were not tightly sealed.

12.12.2005 (41)

Species : other algae: Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)
Endpoint : other: Freshwater alga growth inhibition test
Exposure period : 72 hour(s)
Unit :
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2006
GLP : yes
Test substance : other TS: Diisopropylether (CAS No. 108-20-3)

Method : Statistical Method:
Non-parametric analyses were performed on all growth rate and yield data to estimate NOEC values. A non-parametric analysis of variance was performed on the ranks of the raw data values if both the non-transformed raw data and the transformed data exhibited non-normality or inequality of variance. ErC50 and EyC50 estimates were calculated using a logistic (sigmoid-shaped) model fit to the data with percent inhibition as the dependent variable and concentration as the independent variable. All statistical analyses were performed with SAS for Windows.
Remark : Year (guideline): 2006
Year (study performed): 2007
Result : Test acceptability criteria were met for this study. The number of algal cells in the control at test termination was greater than 16 times the number initially inoculated which verified logarithmic phase growth. The coefficient of variation for daily growth rates in the control replicates during the course of the test did not exceed 35%. The coefficient of variation of average specific growth rates during the whole test period in control replicates did not exceed 7%. There were at least one test concentration exhibiting a less than 50% decrease in growth and one test concentration exhibiting a greater than 50% decrease in growth relative to the control.

Test endpoints at 72 hours based on initial measured concentrations:

EC
Type
EC Value
(mg a.i./L)

95% Confidence Limits
(mg a.i./L)
NOEC
(mg a.i./L)

ErC10
ErC20
ErC50

EyC10
EyC20
EyC50
367
431
566

282
316
385
335 to 399
401 to 461
543 to 590

265 to 298
305 to 327
383 to 388

194

194

Initial measured conc. (mg a.i./L)	72 h % change	72h Mean cell density (cells/mL x 104)
Control	---	118
29.8	+11	131
59.1	+17	138
108	+9	129
194	-3	114
377	-46	64
816	-99	1.1

After 72 hours of exposure, mean cell density in the control was 118 ´ 104 cells/mL, or 236 times the initial cell density.
Measured DIPE concentrations at 0 hour were 29.8, 59.1, 108, 194, 377, and 816 mg a.i./L or 75 to 91% of nominal concentrations. Measured concentrations at 24 hours were 26.8, 51.9, 98.7, 189, 342, and 675 mg a.i./L or 68 to 81% of nominal concentrations. At 48 hours, measured concentrations were 24.2, 53.2, 100, 200, 352, and 719 mg a.i./L or 70 to 82% of nominal concentrations. Measured concentrations at 72 hours were 26.2, 52.1, 96.9, 188, 345, and 728 mg a.i./L or 69 to 88% of nominal concentrations. Measured concentrations at 24, 48, and 72 hours ranged from 81 to 103% of the initial measured concentrations. The measured concentration in the 33 mg a.i./L abiotic sample at 72 hours was 28.9 mg a.i./L, or 88% of the nominal concentration, indicating DIPE was not incorporated into algal biomass. No residues of DIPE were detected in the controls above the MQL of 0.404 mg a.i./L. The analytical results indicated DIPE was stable under test conditions. Initial measured concentrations were used to calculate endpoints since the measured concentrations were not ±20% of the nominal concentrations but were ±20% of the initial measured concentration.

Source : IPA Panel, American Chemistry Council
Test condition : Test solutions were prepared on a volume to volume basis by direct

addition of the test substance to 1.0 L of freshwater algal medium supplemented with 500 mg NaHCO3/L (ASTM, 1997, Standard Guide for Conducting Static 96-h Toxicity Tests with Microalgae. ASTM E1218-97a). Test solutions were corrected for purity and density of the test substance. Treated test solutions were prepared by addition of 0.046, 0.090, 0.18, 0.35, 0.69, and 1.4 mL of DIPE to 1.0 L of freshwater algal medium resulting in nominal concentrations of 33, 65, 130, 250, 500, and 1,000 mg a.i./L. The control solution consisted only of freshwater algal medium with 500 mg NaHCO3/L.

Algal medium was prepared by the addition of appropriate reagent grade salts to autoclaved laboratory reagent water. Laboratory reagent water was produced by passing reverse-osmosis water through a series of deionization tanks, a laboratory water purification system consisting of carbon, de-mineralization, and organic adsorption cartridges, and then through a 0.2-mm filter. After preparation, the medium was pH-adjusted to 7.5 ± 0.1 using 0.1 N HCl and filtered through a 0.45-µm Millipore® filters.

Tests were conducted in 125-mL Erlenmeyer flasks filled so that there was minimal headspace in the flask, and each flask was sealed with Teflon-lined screw cap. The control was replicated six times (replicates A, B, C, D, E, F) for cell counts and analytical samples at test termination. Each test substance treatment was replicated three times (replicates A, B, C) for cell counts and analytical samples at test termination. Two additional test replicates were prepared for the control and each test substance treatment and used for analytical samples and water quality measurements at 24 and 48 hours. Each replicate contained 140 mL of test solution. An additional replicate (replicate D) of the lowest test substance treatment was also prepared and used to evaluate the potential for incorporation of test substance into algal biomass in the inoculated flasks. At test initiation, all replicates of the controls and all but the lowest test substance treatment replicate D were inoculated with 1.0 mL of an algal concentrate containing approximately 7 ´ 105 cells/mL, resulting in a final density of approximately 5.0 ´ 103 cells/mL for each flask. Replicates were inoculated with algae within 30 minutes after test solution preparation. At 24, 48, and 72 hours (±1 hour), cell density was measured in replicates A through F of the control as well as replicates A, B, and C of each test substance treatment by direct microscopic counting with a hemacytometer. Test flasks were maintained at 24 ± 2°C in a temperature controlled environmental chamber under continuous cool-white fluorescent lighting. Light intensity was measured daily. The flasks were swirled on an orbital shaker table at 100 rpm throughout the test.

The parent stock of Pseudokirchneriella subcapitata, formerly known as Selenastrum capricornutum, was obtained from the Department of Botany, Culture Collection of Algae at the University of Texas at Austin. The parent stock was identified as Selenastrum capricornutum. Prepared cultures were maintained in a temperature-controlled environmental chamber under continuous light. Periodically, new cultures were cloned from an existing culture derived from the parent stock. All cultures were maintained under the same conditions as those used for testing. The algal culture used for this test was 4 days old at test initiation and the biomass had increased exponentially (i.e., specific growth rate of 1.2 day-1) during the culture period.

Test solution temperature, measured at 0, 24, 48, and 72 hours, ranged from 22.3 to 23.5°C. Continuous temperature recording within the environmental chamber ranged from 24.0 to 24.5°C. Test solution pH ranged from 7.6 to 7.7 at 0 hour. Test solution pH at 24, 48, and 72 hours ranged from 7.6 to 7.9, 7.8 to 8.5, and 7.9 to 9.5, respectively, in biological replicates. At test initiation and during the exposure, all test solutions appeared clear with no color associated with the test substance, and no

visible precipitates, surface films, or undissolved test substance.

Concentrations of DIPE were measured by gas chromatography (GC) using a flame ionization detector (FID). Sample analysis was performed using a purge and trap autosampler and sample concentrator. The minimum quantifiable limit (MQL) was 0.404 mg a.i./L. Recoveries from quality control fortifications ranged from 94 to 109 % of the nominal concentrations. Concentration of DIPE in test solutions was measured in samples collected at 0, 24, 48, and 72 hours of the definitive test. Samples were centrifuged and an appropriate volume of supernatant was diluted with laboratory reagent water such that the expected final concentration would fall within the range of analytical reference standards.

The pH in the control after 72 hours increased 1.8 units, exceeding the 1.5 units specified in the protocol. The increase of more than 1.5 pH units in the control was the result of cell growth of 236 times the initial cell density and the use of sealed test flasks with minimal headspace, necessary to maintain the exposure concentrations for a volatile test substance, prevented adequate CO2 exchange. The deviation does not affect the study integrity or interpretation of the test results. The control cell growth was not limited by CO2 depletion or increasing pH and did meet the growth acceptability criteria.

Conclusion : The NOEC for growth rate at 72 hours was 194 mg a.i./L. The 72-hour ErC50 was 566 mg a.i./L (95% confidence limits: 543 to 590 mg a.i./L). The NOEC for yield at 72 hours was 194 mg a.i./L. The 72-hour EyC50 value was 385 mg a.i./L (95% confidence limits: 383 to 388 mg a.i./L).

Reliability : (1) valid without restriction
02.02.2008 (38)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	
Vehicle	:	other: None; administered undiluted
Doses	:	
Method	:	other: Similar to OECD 401
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl ether (CAS No. 108-20-3)
Method	:	Administered orally to nonfasted rats. LD50 calculated by the method of Litchfield and Wilcoxon [1949]. Similar to OECD 401.
Remark	:	Test type: Acute oral toxicity Year: Prior to 1971 No. of animals/dose: 6 male for young adult and older adult 6 - 12 male and female for 14-day old rats Route of administration: Oral gavage Dose level: Variable Dose volume: Variable Control group included: No, but none needed
Result	:	14-day old: LD50 6.4 ml/kg [approx 4.5 g/kg] young adults: LD50 16.5 ml/kg [approx 11.6 g/kg] Older adults: LD50 16.0 ml/kg [approx 11.2 g/kg] G/kg dose based on a density of 0.72 g/ml
Test condition	:	Rats were observed for up to 7 days after dosing.
Test substance	:	Diisopropyl ether (CAS No. 108-20-3) Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '- Source/purity of test material is not specified, but stated to be analytical grade meeting ACS specifications.
Conclusion	:	DIPE, when administered to adult male Sprague-Dawley rats, had an acute oral LD50 of >10 g/kg. 14-day immature rats were considerable more sensitive [LD50 4.5 g/kg].
Reliability	:	(2) valid with restrictions Not GLP but conducted at a reputable laboratory [Abbot Laboratories, Chicago].

01.11.2005 (23)

Type	:	
Value	:	
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	no data
Number of animals	:	6
Vehicle	:	other: none reported
Doses	:	8.2, 7.2, 6.0, 5.2, 3.3, 1.62 g/kg
Method	:	other: Similar to OECD 401
Year	:	
GLP	:	no

Test substance	:	other TS: Diisopropyl ether (CAS No. 108-20-3)
Remark	:	Test type: Acute oral toxicity Year: Prior to 1939 Route of administration: Oral Dose levels: 8.2, 7.2, 6.0, 5.2, 3.3, 1.62 g/kg Dose volume: Variable Control: No - none needed
Result	:	Minimal lethal dose between 7 - 9 ml/kg The symptoms noted were lack of coordination and unsteadiness at onset followed by a slight narcosis. In the animals that died the narcosis progressed towards a deep narcosis with loss of corneal reflex and evidences of depressant action on the medulla appeared, respiration became progressively slower, irregular and variable in amplitude and drop in body temperature till respiration failed. In the surviving animals, no effect on HB, erythrocyte count, total and differential leukocyte count was observed. No delayed toxicity was observed during the recovery period of 4 months after treatment.
Test substance	:	Diisopropyl ether (CAS No. 108-20-3) Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '- Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide nor added inhibitor.
Conclusion	:	The test article, when administered orally as received to New Zealand white rabbits had a minimal lethal dose of 7 - 9 ml/kg [approx 5 - 6.5 g/kg].
Reliability	:	(2) valid with restrictions Not conducted by GLP but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (26)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	
Value	:	
Species	:	guinea pig
Strain	:	other: not specified
Sex	:	no data
Number of animals	:	
Vehicle	:	other: none
Doses	:	0.3%; 1%; 3%; 6% in air
Exposure time	:	
Method	:	other: not specified
Year	:	
GLP	:	no
Test substance	:	other TS: Diisopropyl ether (CAS No. 108-20-3)
Remark	:	Test type: Acute inhalation toxicity Year: Prior to 1939 No. animlas/sex/group: One to two animals per dose Route of administration: Inhalation Dose level: 0.3%; 1%; 3%; 6% in air Dose volume: N/A Control: No
Result	:	0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action 1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia 6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr
Test condition	:	1 or 2 hrs or until death [6%]
Test substance	:	Diisopropyl ether (CAS No. 108-20-3) Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane],

2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

Conclusion : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

Reliability : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (26)

Type :
Value :
Species : rabbit
Strain : New Zealand white
Sex : no data
Number of animals :
Vehicle : other: none
Doses : 0.3%; 1%; 3%; 6% in air
Exposure time :
Method : other: not specified
Year :
GLP : no
Test substance : other TS: Diisopropyl ether (CAS No. 108-20-3)

Remark : Test type: Acute inhalation toxicity
Year: Prior to 1939
No. animlas/sex/group: One to two animals per dose
Route of administration: Inhalation
Dose level: 0.3%; 1%; 3%; 6% in air
Dose volume: N/A
Control: No

Result : 0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action
1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia
6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr

Test condition : 1 or 2 hrs or until death [6%]

Test substance : Diisopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

Conclusion : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

Reliability : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (26)

Type :
Value :
Species : monkey
Strain : other: Macacus rhesus
Sex : female
Number of animals :
Vehicle : other: none
Doses : 0.3%; 1%; 3%; 6% in air
Exposure time :
Method : other: not specified
Year :
GLP : no
Test substance : other TS: Diisopropyl ether (CAS No. 108-20-3)

Remark : Test type: Acute inhalation toxicity

Year: Prior to 1939
No. animlas/sex/group: One to two animals per dose
Route of administration: Inhalation
Dose level: 0.3%; 1%; 3%; 6% in air
Dose volume: N/A
Control: No

Result : 0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action
1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia
6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr

Test condition : 1 or 2 hrs or until death [6%]

Test substance : Diisopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

Conclusion : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

Reliability : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (26)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value :
Species : rabbit
Strain : New Zealand white
Sex : no data
Number of animals :
Vehicle : other: none
Doses : variable
Method : other: Similar to OECD 402
Year :
GLP : no
Test substance : other TS: Diisopropyl ether (CAS No. 108-20-3)

Remark : Test type: Acute dermal toxicity
Year: Prior to 1939
No. of animals/sex/group: Unspecified
Route of administration: Dermal
Dose level: variable
Control: No

Result : No deaths or systemic effects were reported. In rabbits dermal unoccluded LD50 > 2.0 g/kg. The actual dose applied was much higher, but continued to evaporate from the skin during application.

Test condition : The material was continuously dripped onto the shaved skin to keep it wet for one hour, while continuously evaporating. 150 ml of material was used.

Test substance : Diisopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

Conclusion : The test article, when administered dermally to New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg.

Reliability : (2) valid with restrictions
Not GLP but conducted at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (26)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

Type	:	other: In vitro chemical reactivity assay, surrogate for respiratory sensitization
Species	:	other: No animals; in vitro chemical assay
Number of animals	:	0
Vehicle	:	other: None
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other: No guideline available
Year	:	1990
GLP	:	no
Test substance	:	other TS: Diisopropyl ether (CAS No.108-20-3)
Remark	:	Route of administration: N/A Sex: N/A Dose level: N/A Dose volume: N/A Control group included: Positive and negative controls included
Result	:	Diisopropanol was negative in this in vitro assay for potential respiratory sensitization. The assay gave positive responses with several known respiratory sensitizers.
Test condition	:	A method for monitoring chemical reactivity in aqueous solutions, at neutral pH and 37 degrees C, was developed. The chemical was allowed to react with a lysine-containing peptide, and the reaction was monitored with high-performance liquid chromatography. Simple acids, bases, and solvents did not react with the peptide, whereas isocyanates, anhydrides, and chloramine-T, substances well known for their sensitizing and asthma inducing properties, did. Thus a positive test strongly suggested that the chemical had the potential to act as a hapten and cause sensitization when inhaled.
Test substance	:	Diisopropyl ether (CAS No.108-20-3) Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '- Source/purity not specified.
Conclusion	:	Di-isopropanol was negative in this in vitro assay.
Reliability	:	(2) valid with restrictions Not conducted by GLP; research method not accepted by regulatory agencies; in vitro surrogate for respiratory sensitisation.

01.11.2005 (46)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation

Exposure period	:	6 hours/day
Frequency of treatm.	:	5 days/week for ~13 weeks
Post exposure period	:	
Doses	:	0, 480, 3300, or 7100 ppm
Control group	:	other: yes (untreated & sham-exposed)
NOAEL	:	= 480 ppm
Method	:	EPA OTS 798.2450
Year	:	1996
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : Statistical method:
Statistical analyses of numerical data included ANOVA and Tukey's studentized range test for data on serum chemistry. Duncan's multiple range test was used for hematology and body weights to assess statistically significant differences between control and exposed groups.

Remark : Male and female rats were acclimated for 2 weeks before initiation of exposures that began at ~8 weeks of age. Exposed animals were individually housed in 1-m3 inhalation chambers. Untreated control animals were housed in a separate room in identical caging. Room environment was set to 20-22ºC and 40-60% relative humidity. Lights were on a 12/12-hr light/dark cycle. Food and water were provided ad libitum except during exposures.

Vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy.

The primary endpoints during the course of exposures were individual body weights recorded weekly and clinical signs recorded daily except on weekends.

Following the last exposure, rats were fasted overnight and weighed; blood samples were obtained via the orbital sinus using light anesthesia. Samples were used to determine values for WBC, RBC, Hgb, Hct, MCV, MCH, MCHC, platelets, and differential counts. Glucose, urea nitrogen, total protein, albumin, globulin, A/G ratio, sorbitol dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, creatinine, cholesterol, triglycerides, uric acid, Cl, Ca, Na, K, and P. Following the collection of blood samples, all animals were euthanized with sodium pentobarbital (i.p.) and exanguinated. Per the EPA 798.2450 protocol, approximately 40 tissues (including ovaries and uterus) were collected for histopathology and organs were weighed. Histopathology was performed on all high-dose and control animals and any gross lesions from all doses. Testis and associated tissues were preserved whole in 10% buffered formalin except for the left cauda epididymis of 10 rats in both control groups and the highest test group; epididymides were evaluated for morphology and number of sperm. The left testis in these groups was weighed and used for determination of number of testicular spermatids.

Type: 90-Day Subchronic
Species/strain: Rat/Sprague-Dawley; Tac:N(SD)fBR
No./sex/dose: 14/sex/group
Vehicle: None
Method: USEPA 1984, 40CFR Part 798:2450

Result	:	DIPE did not adversely affect clinical signs body weight, serum chemistry, hematology, or the number of sperm or spermatids. Exposure to males at 7100 ppm resulted in hypertrophy of liver cells associated with increased liver weight and in increased kidney weight with an increased incidence of hyaline droplets in proximal tubules of the kidney. Females had increased weight of both liver and kidney, although kidney increased only in relation to sham-exposed controls and no morphologic changes were observed in either organ. At 3300 ppm, weights of liver and kidney were increased in males; the liver weights were increased in females only compared to sham-exposed controls and not untreated controls. No morphologic abnormalities were observed. No changes were observed with 480 ppm.
Test substance	:	Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.
Conclusion	:	NOAEL = 480 ppm
Reliability	:	(2) valid with restrictions GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (8)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	6 hours/day
Frequency of treatm.	:	5 days/week for ~13 weeks
Post exposure period	:	
Doses	:	0, 450, 3250, or 7060 ppm
Control group	:	other: yes (sham-exposed)
Method	:	other: USEPA 1984, 40CFR Part 798:6050, 6400, and 6200
Year	:	1997
GLP	:	no data
Test substance	:	other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method	:	Statistical method: All statistical analyses were performed with SAS software. Body weights, rectal temperatures fore- and hindlimb grip strengths, the number of rears, and motor activity were analyzed by a one-way analysis of variance followed by Duncan's multiple range test. The remaining data from the FOB were analyzed by Fisher's exact test using an extended contingency table containing all four groups of at given sex at a specified time. If a significant difference occurred for a given parameter, Fisher's exact test was used to directly compare each group individually against the control. Brain weights, lengths and widths, were analyzed by Student's t-test.
Remark	:	Male and female rats were acclimated for 2 weeks before initiation of exposures that began at ~8 weeks of age. Sham-exposed and exposed animals were individually housed in 1-m3 inhalation chambers except during behavioral testing, when they were placed in another room overnight and evaluated the following day. Room environment was set to 20-22ºC and 40-60% relative humidity. Lights were on a 12/12-hr light/dark cycle. Food and water were provided ad libitum except during exposures. Exposure vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1-m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy. Exposures were stagger-started over a 5-day period with 16 animals, 2/sex/group, receiving their first exposure on each of 5 consecutive days.

The rats were observed for signs of toxicity daily prior to initiation of exposures, and individual body weights were recorded weekly.

During weeks of Functional Observation Battery (FOB) evaluation, four rats/group would be removed from the inhalation chamber and housed separately overnight and evaluated on the following day between the hours of 7:30 a.m. and 11:00 a.m. The process was repeated for each consecutive day until all rats were evaluated. The rats were evaluated with minimal disruption to the exposure schedule and with a manageable number of rats per day, 16 on any given day. The animals were evaluated in an FOB followed by a determination of motor activity prior to initiation of exposure; the FOB following 2, 4, 8, and 13 weeks of exposures, and for motor activity following 4, 8, and 13 weeks of exposures. Following the final determination of motor activity, the animals were anesthetized, intravascularly perfused, and the brain, spinal cord, and peripheral nerves removed for microscopic examination.

The FOB consisted of initially observing home-cage positioning, posture, and reaction to removal from the cage. This was followed by evaluation for exophthalmus/palpebral closure, lacrimation, salivation, pupillary response, palpebral reflex, and pinna reflex. These observations were scored by type and intensity. The animals were then observed for open field behavior. Piloerection, respiratory rate, tremors, convulsions, posture, gait, ataxic gait, tail elevation, unperturbed activity level, vocalization, number of rears, fecal balls, and urine pools were all recorded during the open-field observations. Reactions to the approach of a pencil, finger snap, and tail pinch were ranked and recorded. Finally, fore- and hindlimb grip strength , rectal temperature , and body weight were measured. Automated motor activity was assessed for 30 minutes in figure-eight mazes after the completion of the FOB.

Following the last FOB and motor activity evaluation, the rats were anesthetized with heparinized sodium pentobarbital (i.p.). The thoracic cavity was opened and the animals were infused with phosphate-buffered gluteraldehyde through the left ventricle. The perfused brain, spinal cord, and sciatic nerve with its tibial, sural, and peroneal divisions were removed. The brain and nerve tissues were processed for embedding in paraffin or glycol methacrylate (dorsal root ganglia and peripheral nerves) and sectioned for light or electron microscopic pathologic evaluation.

Type: 90-Day Neurotoxicity
Species/strain: Rat/Sprague-Dawley; Tac:N(SD)fBR
No./sex/dose: 10/sex/group
Vehicle: None
Method: USEPA 1984, 40CFR Part 798:6050, 6400, and 6200

Result : Motor activity in a figure-eight maze and unperturbed activity in the FOB were decreased at week 4 in females exposed to 7060 ppm; activity in the FOB was also decreased in females exposed to 450 ppm at week 4. Other changes in the FOB appeared to be minor, and no changes were observed during microscopic examination of tissues from the nervous system.

Test substance : Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.

Conclusion : Inhalation exposures to DIPE at concentrations as high as 7060 ppm for 13 weeks resulted in few observable effects on the nervous system.

Reliability : (2) valid with restrictions
GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (35)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium
Test concentration	:	Up to 8000 ug/ml in the pre-incubation mix
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Similar to OECD Guideline 471
Year	:	1988
GLP	:	no data
Test substance	:	other TS: Diisopropyl ether (CAS No. 108-20-3)
Remark	:	Strains tested: Salmonella typhimurium tester strains TA98, TA100, TA1535, TA1537, TA1538 Exposure method: Preincubation assay for volatile compounds [Brooks and Dean 1981] Test Substance Doses/concentration levels: Up to 8000 ug/ml in the pre-incubation mix Metabolic activation: With and without (S9 fraction mix of livers of Aroclor 1254 pretreated rats) Vehicle: Tween 80/ethanol Tester strain, activation status, Positive Controls and concentration level: Not stated Statistical analysis: Mean revertant colony count and standard deviation were determined for each dose point. Dose Rangefinding Study: Cytotoxicity study S9 Optimization Study: No
Result	:	DIPE did not induce reverse gene mutation in any strain. The test substance was not genotoxic in this assay with or without metabolic activation.
Test substance	:	Diisopropyl ether (CAS No. 108-20-3) Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '- Source/purity not specified.
Conclusion	:	Under the conditions of this study, the test material was not mutagenic.
Reliability	:	(2) valid with restrictions Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (5)

Type	:	Sister chromatid exchange assay
System of testing	:	Chinese hamster ovary cells
Test concentration	:	Up to 1200 ug/ml
Cycotoxic concentr.	:	
Metabolic activation	:	without
Result	:	negative
Method	:	other: Similar to OECD Guideline 473
Year	:	1984

GLP : no data
Test substance : other TS: Di-isopropyl ether (CAS No. 108-20-3)

Remark : Test type: Chromosome damage

Exposure method: For volatile compounds

Metabolic activation: Metabolic activation S9 was not added because liver cells are metabolically competent

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Cultured CHO cells were grown in 80 cm2 flasks for 24 hr before compound treatment. Treatment periods were 5 hr in the presence of S9 mix and 24 hr in the absence of S9. Colcemid was added to all cultures 22 hr after the initial treatment. After a further 2 hr, the cells were trypsinized, resuspended in hypotonic solution and then fixed, before spotting onto slides. Cell preparations were then stained with Giemsa. The slides were randomly coded and 100 cells from each culture were analyzed microscopically. Mitotic index estimations were also made. The positive controls were ethylmethanesulfonate [-S9] and cyclophosphamide [+S9].

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: No

Result : DIPE did not induce chromosomal damage in CHO cells. The test substance was not genotoxic in this assay.
Test substance : Di-isopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%
Conclusion : Under the conditions of this study, the test material was not mutagenic.
Reliability : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (4)

Type : DNA damage and repair assay
System of testing : Rat liver cells
Test concentration : Up to 1200 ug/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: Similar to OECD Guideline 476
Year : 1984
GLP : no data
Test substance : other TS: Di-isopropyl ether (CAS No. 108-20-3)

Remark : Test type: Chromosome damage

Strains tested: RL4

Metabolic activation: Metabolic activation S9 was not added because liver cells are metabolically competent.

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Cultured rat liver cells were grown and treated on glass microscope slides contained in 100 ml glass Leighton tubes. After 22 hr exposure to test compound or solvent, colcemid was added to each culture. After a further 2 hr, the slides were removed, subjected to hypotonic treatment followed by fixation and stained with Giemsa. The preparations were randomly coded and 100 cells from each culture were analyzed microscopically. The positive control was 7,12-dimethylbenzanthracenene.

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: None needed

Result : DIPE did not induce chromosomal damage in rat liver cells. The test substance was not genotoxic in this assay.

Test substance : Di-isopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%

Conclusion : Under the conditions of this study, the test material was not mutagenic.

Reliability : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (4)

Type : Gene mutation in Saccharomyces cerevisiae
System of testing : Saccharomyces cerevisiae
Test concentration : Up to 8000 ug/ml in the pre-incubation mix
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: Similar to OECD Guideline 481
Year : 1984
GLP : no data
Test substance : other TS: Di-isopropyl ether (CAS No. 108-20-3)

Remark : Test type: Yeast mitotic gene conversion

Strains tested: JD1

Exposure method: [Brooks and Dean 1981]

Metabolic activation: With and without (S9 fraction mix of livers of Aroclor 1254 pretreated rats)

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Yeast cells were grown in log-phase, washed and resuspended in 2/5 strength YEPD broth at a concentration of 1 X 107 cells/ml. The suspension was divided into 1.9 ml amounts in 30 ml universal containers and 0.1 ml of test compound solution was added. For experiments with metabolic activation [+S9], 0.1 ml of DIPE was added to0 1.6 ml of yeast cell suspension, together with 0.3 ml of S9 mix. Initially a range of concentrations of DIPE was tested up to 5 mg/ml if solubility allowed. A

second experiment was performed based on these results and taking into account cell viability. The cultures were incubated with shaking at 30 C for 18 hr. Aliquots were plated onto the appropriate culture media for selection of mitotic gene convertants and cells surviving the treatment. Mitotic gene conversion may be scored by supplementing the minimal medium with histidine to score tryptophan prototrophs, and with tryptophan to score histidine prototrophs. Control plates were set up with solvent alone and with the positive control compounds 4-nitroquinoline oxide and cyclophosphamide.

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: No

Result : DIPE did not induce mitotic gene conversion I yeast. The test substance was not genotoxic in this assay with or without metabolic activation.

Test substance : Di-isopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%

Conclusion : Under the conditions of this study, the test material was not genotoxic.

Reliability : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (4)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

Type : Chronic Study
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : Oral gavage
Exposure period : 78 weeks
Frequency of treatm. : 4 days/week for 78 weeks
Post exposure period : Up to 85 weeks post treatment (last animal death)
Doses : 250 and 1000 mg/kg b-wt
Control group : Yes, extra virgin olive oil
NOAEL : Not applicable
Method : Non-conventional
Year : 2002
GLP : no data
Test substance : Diisopropyl Ether (CAS No. 108-20-3)
Purity : 98 %
Method : DIPE was assessed in a long term, non-conventional gavage study in rats at dose levels of 0, 250 and 1000 mg/kg/day, 4 days a week for 78 weeks. All animals were observed until spontaneous death and the experiment ended after 163 weeks.
Result : There were no significant differences between treated and control groups in daily food or water consumption, body weight, behavior or non-neoplastic pathological changes. Survival was decreased in treated males compared to controls between the 56^{th} and 88^{th} weeks of age. A

statistically significant increase in total malignant tumours was reported in males at the low dose only and a significant trend in females of both treated groups. The incidence of carcinomas of the ear duct in males was statistically significant but was not dose related. A statistically significant increase in combined hemo/lympho-reticular neoplasias (% tumor-bearing animals) was seen in males and females at both dose levels. The increase in tumor incidence was not statistically significant for low dose males but the trend was. Significance was not reported for individual tumours (% tumor bearing animals) or for individual types of lymphoma or leukemia.

Conclusion : The findings of this "lifetime" carcinogenicity study in rats are equivocal.

Remark : There were a number of deficiencies in design and reporting of this non-conventional study, which made interpretation difficult. These included the maintenance of the animals to their natural death (usually studies are terminated at the end of a predetermined exposure period and/or survival level), lack of detail in reporting statistical significance of tumor incidence (e.g., combined lymphoma and leukemia), and limited reporting of survival. There was no indication of or comparison to historical control data. For these reasons the findings and the significance of such are questionable and are considered equivocal.

Statistical Methods : Not Reported

Reliability : (4) Not Assignable
The reliability of this study is rated a 4 (not assignable) because of the deficiencies in the study design and reporting of this non conventional study as explained in the remark section.

27.2.2008 (49)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 6 hr/day
Frequency of treatm. : Gestation Days 6-15
Duration of test : 20 days
Doses : 0, 430, 3095, or 6745 ppm
Control group : other: yes (untreated & sham-exposed)
other: NOEL Maternal : = 430 ppm
other: NOEL Pup : = 430 - ppm
Result : Maternal NOEL: 430 ppm; Pup NOEL: 430 ppm
Method : EPA OTS 798.4350
Year : 1996
GLP : no data
Test substance : other TS: Diisopropyl Ether (CAS No. 108-20-3)

Method : Statistical method:
Statistical analyses of numerical data included ANOVA and Tukey's studentized range test for data on serum chemistry. Duncan's multiple range test was used for hematology and body weights to assess statistically significant differences between control and exposed groups. Data on the maternal biophase, cesarean sections, and fetuses were evaluated by ANOVA followed by group comparisons using Fisher's exact or Dunnett's test.

Remark : Nulliparous females were housed with males in a 1:1 ratio and observed daily for evidence of breeding activity. Females positive for sperm plug and for sperm in the vaginal lavage fluid were considered to be at day 0 of

gestation and were individually housed. The females were then randomly distributed to 5 groups of 22 animals each: untreated controls, sham-exposed controls, and 3 groups exposed to vapors of DIDP at 430, 3095, or 6745 ppm for 6 hr/day on gestation days (GD) 6-15.

Vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy.

Sham-exposed and test animals were housed in their exposure chambers throughout the exposure period; untreated controls in a separate room. Food and water were not available during the 6 -hour exposure periods but were available ad libitum at all other times. All animals were observed daily. Body weights were recorded on days 0, 6, 13, 16, and 20. Food consumption was measured on GD 6, 13, 16, and 20. Females were sacrificed on GD 20 by diethyl ether overexposure followed by exsanguination. Serum samples from the descending aorta were analyzed for glucose, urea nitrogen, total protein, albumin, globulin, A/G ratio, sorbitol dehydrogenase, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, creatinine, cholesterol, triglycerides, uric acid, Cl, Ca, Na, K, and P. All organs were examined grossly. The number of corpora lutea per ovary and the gravid uterine weights were recorded. Uterine contents were examined and the numbers of implantation sites, early and late resorptions, and live and dead fetuses were recorded. The gender of each fetus was recorded. Fetuses were weighed and examined for gross anomalies. Fetuses of each litter were equally distributed between two groups; half were fixed in Bouin's solution and examined for visceral anomalies and the remaining fetuses were fixed in 95% ethanol and examined for skeletal anomalies after differential staining for cartilage and bone.

Dams exposed to 6745 ppm had a slight reduction in body weight gain and a significant decrease in food consumption. A concentration-related increase in the incidence of rudimentary 14th ribs was observed (statistically significant at 3095 and 6745 ppm) but the relevance of the finding was uncertain. There was no apparent toxicity, either maternal or fetal, at the lowest exposure concentration, 430 ppm.

Type: Developmental Toxicity
Species/strain: Sprague-Dawley; VAF/Plus Crl:CD(SD)BR
No./dose: 22/group
Vehicle: None
Method: USEPA 1984; 40CFR Part 798:4350

Result : Maternal NOEL: 430 ppm
Pup NOEL: 430 ppm
Test substance : Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.
Conclusion : DIPE is not a teratogen.
Reliability : (2) valid with restrictions
GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (8)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

Type : other: Sensory Irritation in Humans

Method : Non-guideline.
Remark : Species/strain: Humans
Sex: Male and female
Number/sex/group: Average of 12
Route of administration: Inhalation
Vehicle: None
Control: No
Year: Prior to 1946
GLP: No
Result : 300 ppm: 35% of the subjects objected to this solvent because of the unpleasant odor rather than irritation.
500 ppm: there was a sensory response that was acceptable to the majority of subjects.
Test condition : Subjects were exposed for 15 minutes and olfactory fatigue and irritation of mucous membranes were reported. "Motion pictures were shown to occupy the subject's attention and divert their thoughts from the atmospheric contamination to which they were exposed."
Test substance : Diisopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be technical grade product.
Conclusion : DIPE does not appear to be a sensory irritant at concentrations up to 500 ppm, but it does have an unpleasant odor at this concentration.
Reliability : (2) valid with restrictions
Not GLP but conducted at a reputable laboratory [Harvard School of Public Health, Boston].

01.11.2005 (39)

Type : other: Sensory irritation in humans

Method : Non-Guideline.
Remark : Species/strain: Young adult humans [University of California staff and medical students]
Sex: Not specified
Number/sex/group: Not specified
Route of administration: Inhalation
Vehicle: None
Control: No
Year: 1955
GLP: No
Result : Numbers of subjects with degree of effect

Concentration	400 ppm	800 ppm
Number subjects:	7	7
Eye irritation:	7 absent	3 absent, 3 slight, 1 mod.
Nose irritation:	5 absent, 2 slight	2 absent, 5 slight
Pulmonary discomfort:	7 absent	4 absent, 3 slight
Olfactory cognition :	1 slight, 6 mod.	4 mod., 3 severe
CNS effects :	7 absent	7 absent

Test condition : Exposures were conducted in a whole-body chamber approximately 7700 l

equipped with a fan. Exposures were made in a static atmosphere generated by vaporizing a predetermined quantity of test solvent from a hot surface. Five minutes were allowed for evaporation and equilibration, and subjects were exposed for 5 minutes, during which time they noted the degree of subjective responses at one-minute intervals.

Test substance : Diisopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with purity of 98% or better, provided by Shell Chemical Corporation.

Conclusion : 400 ppm: 5 mins of inhalation exposure caused no eye irritation, none to slight nose irritation, no pulmonary discomfort, olfactory recognition but no central nervous system effects.

800 ppm: 5 mins of inhalation exposed caused slight eye and nose irritation, none to slight pulmonary discomfort, definite olfactory recognition but no central nervous system effects.

Reliability : (2) valid with restrictions
Not GLP but conducted at a reputable laboratory [University of California School of Medicine].

01.11.2005 (22)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT